BIOC 482/552: Structural Biology

Credits: 3

Prerequisites: Concurrent or prior biochemistry; and freshman physics or equivalent

Date/Time/Place: Spring 2021, 9:45-10:40 AM, MWF, Keck Hall 107 MW and GEO 130 Fridays

Instructors: George N. Phillips (georgep@rice.edu), Ed Nikonowicz (edn@rice.edu)
TA: Abigael Kosgei (ajk15@rice.edu) Office hours by appointment.

Textbook/Readings: Lattman and Loll, Protein crystallography: A concise guide. 2008, Johns Hopkins Press (Kindle or Amazon), IUCr On-line dictionary of crystallography (free access),

Course Description: Structural biology plays an important role in defining atomic structures of biomolecules and understanding relationships between structure, dynamics and function. This course will give an introduction to techniques of determining bimolecular structures, X-ray crystallography, NMR, and cryoelectron microscopy and discuss striking examples of the power of structural biology including biomedical examples. It will provide knowledge of techniques used to obtain detailed structural and dynamic information about biological macromolecules. Designed for advanced undergraduates and beginning graduate students in the biological or physical sciences. Students will present short vignettes on interesting structural results and will design and print 3-D models on a color printer as a part of their presentation. There will be two short in-class exams, homework and a presentation with 3-D printer support, but no final exam. BIOC 553 students (graduate students) will be required to give two presentations. Mondays and Wednesdays will be structural biology techniques and examples in biomedicine, Fridays will be practical homework/discussion sections.

Course Objectives and expected learning outcomes:

- To introduce the fundamental theory and the practice of X-ray crystallography and NMR in modern structural biology and biomedicine
- To evaluate the research articles from the primary literature to understand and analyze advanced topics in X-ray crystallography, with an emphasis on fundamental principles, research methodologies, and emerging research topics.
- To improve scientific communication skills through explaining conclusions and methodology to the group and fielding questions.

Grading: Course grade based equally on three components. Homeworks, Exams, Presentation(s).
The presentation will include production of a 3-D printed model of a macromolecule and a 20 minute talk.

Rice Honor Code: Students are required to use proper citations and follow other practices outlined in the Rice Honor Code information on Academic Fraud and Acknowledgement of Sources: http://honor.rice.edu/honor-system-handbook/

Accommodations for students with disabilities: Any student with a documented disability needing academic adjustments or accommodations is requested to speak with the instructor during the first two weeks of class. All discussions will remain confidential. Students with disabilities also should contact Disability Support Services in Allen Center.

Teaching will be offered in person as soon as allowed and recorded for off-line/remote viewing.

Topics to be covered:

Overview of imaging and role of structural methods in modern science
Symmetry (point groups, 2D, 3D, icosahedra: Crystallization of proteins
Diffraction from cyrstalline objects, Reciprocal space
Electron density equation, Phase problem, Patterson function, Heavy atom/direct methods, isomorphous replacement
Molecular replacement, Non-crystallographic averaging, refinement, Laue methods, synchrotrons, phasing
X-ray fiber diffraction, solution scattering
NMR methods of structure determination
High resolution electron microscopy
Molecular Dynamics Simulations
Analysis of electrostatics of proteins
Structure-based drug design

Student and others' presentations on interesting biological systems and 3-d printing of molecules

Preliminary Schedule

Week 1

Jan 25	Introduction to class and requirements
	Brief review of chemical structure of proteins and nucleic acids
Jan 27	Brief overview of crystallography
Jan 29	HW1- PYMOL intro (Geo Lab)

Week 2

Feb 1	Review of complex numbers and operators needed in the class
	Scattering and illustration of how diffraction is the sum of waves
	Comparison of imaging methods in biology.
Feb 3	Lattices, unit cells (Geo Lab)
	Symmetry
	Space groups
	Miller indices
Feb 5	HW2 – scattering and symmetry

Week 3

Feb 8	Diffraction from arbitrary objects, slits and from lattices
Feb 10	Reciprocal Space
	Bragg's Law
	X-ray sources
	Crystal mounting
Feb 12	HW3 1-d transform exercise, X-RayView exercises,

Week 4

Feb 15	Electron density equation
	The Phase Problem
Feb 17	Sprinkle day – no class
Feb 19	HW3 1-d transform exercise

Week 5

Feb 22	Phase problem continued, molecular replacement
	Difference maps

	Refinement and Cross-validation/PDB
	Specialized Maps
Feb 24	Review
Feb 26	Field trip for crystallography lab

Week 6

Mar 1	Diffraction from helices
	Discovery of the double helix and other helical objects
Mar 3	Diffraction from membranes, solutions and examples
Mar 5	Crystallography Exam

Week 7

Mar 8	Sprinkle Day – no class
Mar 10	Basics of NMR
Mar 12	One- and Two-dimensional NMR Experiments

Week 8

Mar 15	Two-dimensional NMR Experiments continued
Mar 17	Structural Constraints from NMR, Integration with MD Simulations
Mar 19	NMR instrument operation

Week 9

Mar 22	The phenomenon of chemical exchange
Mar 24	Relaxation-dispersion and measuring microsecond timescale motions
Mar 26	Additional types of structure constraints:
	Residual dipolar couplings
	Chemical shift tensors
	NMR Problem Set due

Week 10

Mar 29	Dealing with the molecular size problem
	Transverse Relaxation Optimized Spectroscopy
	Random fractional deuteration
Mar 31	Application of NMR to *very* big protein and RNA complexes
Apr 2	NMR exam

Week 11

Apr 5	Electron microscopy**,** Single particle Cryo-EM
Apr 7	Molecular Dynamics Simulations
Apr 9	NAMD Exercise

Week 12

Apr 12	Protein folding – Anfinsen dogma
	Measurement of folding/unfolding
	Anton machine
Apr 14	CASP, Homology Modeling, Alpha-fold
	BLAST
Apr 16	BLAST/homology exercise, finish model to be printed

Week 13

Apr 19	Student presentations
Apr 21	Student presentations
Apr 23	Student presentations

Week 14

Apr 26	Student presentations
Apr 28	Student presentations
Apr 30	Student presentations